**Orally available nonopioid analgesic and nonsteroidal anti-inflammatory drugs (NSAIDs): Usual dosing for adults with pain or inflammation**

| Drug | Optional initial loading dose | Usual analgesic dose (oral) | Maximum dose per day (mg) | Selected characteristics and role in therapy |
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| **Para-aminophenol derivative** | | | | |
| Acetaminophen* (paracetamol, APAP) | None | 325 to 650 mg every 4 to 6 hours<br>Or<br>1000 mg every 6 hours up to three times per day | 3000 mg | ▪ Effective for noninflammatory pain; may be opioid-sparing.<br>▪ Doses <2000 mg per day do not increase risk of serious GI complications.<br>▪ Does not alter platelet functioning.<br>▪ Can cause hepatotoxicity in chronic or acute overdose.<br>▪ Avoid or use a lower total daily dose (maximum 2000 mg per day) in older adults, patients at risk for hepatotoxicity (eg, regular alcohol use, malnourished) or with organ dysfunction.<br>▪ For short-term or one-time use, may use a total dose of up to 4000 mg per day in selected medically supervised patients.<br>▪ Interacts with warfarin (prolongs INR), isoniazid, and CYP450-inducing drugs[¶] (transaminitis).<br>▪ Warn patients about acetaminophen content in combination prescription (eg, oxycodone-acetaminophen) and OTC preparations. |
| **NSAID agents** | | | | |
| **Applies to all nonselective NSAIDs:**<br>▪ Effective for treatment of acute and chronic painful and inflammatory conditions. May decrease opioid requirements. Short-to-moderate-acting NSAIDs (eg, naproxen, ibuprofen) are preferred for most patients.<br>▪ Dose- and age-related risk of gastropathy.<br>▪ May cause or worsen renal impairment.<br>▪ Nonselective NSAIDs reversibly inhibit platelet functioning and can alter cardioprotective effects of aspirin.<br>▪ Avoid NSAIDs in patients with renal insufficiency (CrCl <60 mL/minute), GI bleeding, platelet dysfunction, reduced cardiac output, difficult-to-control hypertension, hypovolemia, hyponatremia, aspirin-sensitive asthma, or cirrhosis.<br>▪ Safety concerns of NSAID use in patients with, or at elevated risk for, cardiovascular disease or thrombotic events are addressed in a separate topic in UpToDate.<br>▪ Use with caution or avoid in patients receiving comedication with anticoagulants, systemic glucocorticoids, lithium, loop diuretics, and other interacting drugs. Drug interactions may be checked using the Lexi-Interact program included with UpToDate.<br>▪ Though some older adults may benefit from a brief course of NSAIDs at the lowest effective dose, use in most older adults should be avoided. Refer to the UpToDate topics on treatment of pain in older adults and older adults with organ dysfunction. | | | | |
| **Salicylate (acetylated)** | | | | |
| Aspirin* | 2600 mg | 325 to 650 mg every 4 to 6 hours | 4000 mg | ▪ Standard for comparison, but now used infrequently for treatment of chronic pain and inflammation.<br>▪ Unlike other NSAIDs, irreversibly inhibits platelet functioning for life of the platelet (7 to 10 days). |
| **Salicylates (nonacetylated)** | | | | |
| Diflunisal | 1000 mg | 500 mg every 8 to 12 hours | 1500 mg | Applies to all nonacetylated salicylates:<br>▪ No significant effect on platelet function at usual analgesic doses.<br>▪ Less frequently associated with GI bleeding than nonselective NSAIDs at usual analgesic doses.<br>▪ Generally tolerated by adults with asthma at lower daily doses: Diflunisal ≤1000 mg, choline magnesium trisalicylate and salsalate ≤2000 mg.<br>▪ Relatively slow onset.<br>▪ 500 mg dose of diflunisal has a comparable analgesic effect with 650 mg acetaminophen or aspirin. |
| Choline magnesium trisalicylate | 1500 mg | 750 mg every 8 to 12 hours | 3000 mg | |
| Salsalate | 1500 mg | 750 to 1000 mg every 8 to 12 hours | 3000 mg | |
| **Propionic acids (phenyl-propionic acid)** | | | | |
| Naproxen* | 500 mg (naproxen base)<br>550 mg (naproxen sodium) | 250 to 500 mg every 12 hours (naproxen base)<br>275 to 550 mg every 12 hours (naproxen sodium) | 1250 mg acute, 1000 mg chronic (naproxen base)<br>1375 mg acute, 1100 mg chronic (naproxen sodium) | ▪ A good choice for treatment of acute or chronic pain and inflammation in most patients if NSAID therapy is indicated.<br>▪ High doses (eg, 500 mg twice daily) may have less cardiovascular toxicity than comparable doses of other NSAIDs.[◇]<br>▪ For the treatment of rheumatologic disorders, total daily dose may be increased to a maximum of 1500 mg base (1650 mg naproxen sodium), when needed.<br>▪ Naproxen sodium has more rapid absorption and onset of effect than naproxen base. |
| Ibuprofen* | 1600 mg | 400 mg every 4 to 6 hours | 3200 mg (acute), 2400 mg (chronic) | ▪ 200 to 400 mg dose has a comparable analgesic effect with 650 mg acetaminophen or aspirin.<br>▪ Short duration of effect.<br>▪ Useful alternative to naproxen in patients without cardiovascular risks. |
| Ketoprofen | 100 mg | 50 mg every 6 hours or 75 mg every 8 hours | 300 mg | ▪ 25 mg dose has a comparable analgesic effect to 400 mg ibuprofen.<br>▪ Short duration of effect. |
| Flurbiprofen | 100 mg | 50 to 100 mg every 6 to 12 hours | 300 mg | ▪ Lozenge preparation available in some countries. |
| Oxaprozin | None | 1200 mg once daily | 26 mg/kg up to 1800 mg (whichever is lower) | ▪ Long duration of effect. |
| **Acetic acids (pyrano-indoleacetic acid)** | | | | |
| Diclofenac | 75 or 100 mg (conventional tablets) | 50 mg every 8 hours | 150 mg<br>Approved maximum daily dose in some countries is | ▪ Diclofenac is also available as a topical patch, solution, and gel for treatment of musculoskeletal pain and osteoarthritis of superficial joints, which may be useful in combination with or as an alternative to |

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| | | | 100 mg | systemic NSAIDs. Refer to the UpToDate topic on initial treatment of osteoarthritis and separate table.<br>▪ Interacts with drugs that are strong inhibitors or inducers of CYP2C9 drug metabolism; use Lexi-Interact to determine specific interactions. |
| Etodolac | 400 to 600 mg | Immediate release: 200 to 400 mg every 6 to 8 hours<br>Extended release: 400 to 1000 mg once daily | Immediate release: 1000 mg<br>Extended release: 1200 mg | ▪ Relatively COX-2 selective at lower total daily dose of 600 to 800 mg.<br>▪ 200 mg dose has a comparable analgesic effect with 400 mg of ibuprofen. |
| Indomethacin | 75 mg | Immediate release: 25 to 50 mg every 8 to 12 hours<br>Controlled release: 75 mg once or twice daily | 150 mg | ▪ Useful for treatment of acute gout and specific types of headache.<br>▪ Potent inhibitory effects on renal prostaglandin synthesis.<br>▪ More frequently associated with CNS side effects (eg, headache) compared with other NSAIDs.<br>▪ Carefully select and monitor patients to reduce risk of renal and cardiovascular toxicities. |
| Tolmetin | 600 mg | 400 to 600 mg every 8 hours | 1800 mg | |
| Sulindac | 300 mg | 150 to 200 mg every 12 hours | 400 mg | ▪ More frequently associated with hepatic inflammation (idiosyncratic or with features of hypersensitivity) compared with other NSAIDs.<br>▪ Sulindac metabolites implicated in the formation of renal calculi; refer to the UpToDate topic on nonselective NSAID adverse effects.<br>▪ Prescribing should be limited to specialists with experience in treatment of chronic pain and inflammation. |
| **Oxicams (enolic acids)** | | | | |
| Meloxicam | 7.5 mg (conventional tablets) | 7.5 to 15 mg once daily | 15 mg | ▪ Long duration of effect; slow onset.<br>▪ Relatively COX-2 selective and minimal effect on platelet function at lower total daily dose of 7.5 mg.<br>▪ Rarely associated with serious cutaneous allergic reactions, including Stevens-Johnson syndrome. |
| Piroxicam | 10 mg | 10 to 20 mg once daily | 20 mg | ▪ A long-acting option for treatment of chronic pain and inflammation poorly responsive to other NSAIDs.<br>▪ Daily doses ≥20 mg increase risk of serious GI complications.<br>▪ Concurrent pharmacologic gastroprotection is suggested.<br>▪ Rarely associated with serious cutaneous allergic reactions, including Stevens-Johnson syndrome.<br>▪ Prescribing should be limited to specialists with experience in treatment of chronic pain and inflammation. |
| **Fenamates (anthranilic acids)** | | | | |
| Meclofenamate (meclofenamic acid) | 150 mg | 50 mg every 4 to 6 hours | 400 mg | ▪ Alternate NSAID choice for treatment of acute or chronic pain, inflammation, and dysmenorrhea.<br>▪ Appears to be associated with higher incidence of GI disturbance (including diarrhea) compared with other nonselective NSAIDs. |
| Mefenamic acid | 500 mg | 250 mg every 6 hours | 1000 mg | ▪ Alternate NSAID choice for treatment of acute pain and dysmenorrhea.<br>▪ Duration of use not to exceed seven days (acute pain) or three days (dysmenorrhea).<br>▪ Anti-inflammatory efficacy is comparatively low.<br>▪ Not indicated for treatment of chronic pain or inflammation. |
| **Nonacidic (naphthylalkanone)** | | | | |
| Nabumetone | 1000 mg | 500 to 750 mg every 8 to 12 hours or 1000 to 1500 mg once daily | 2000 mg | ▪ Moderate duration of effect; slow onset.<br>▪ Relatively COX-2 selective at lower total daily dose of 1000 mg or less.<br>▪ Minimal effect on platelet function at total daily dose of 1000 mg or less. |
| **Selective COX-2 inhibitors§** | | | | |
| Celecoxib | 400 mg | 200 mg daily or 100 mg every 12 hours | 400 mg | ▪ Relative reduction in GI toxicity compared with nonselective NSAIDs.<br>▪ No effect on platelet function.<br>▪ Cardiovascular and renal risks are dose-related and appear similar to those of nonselective NSAIDs.<br>▪ Patients with indications for cardioprotection require aspirin supplement; individuals may require concurrent gastroprotection. |
| Etoricoxib (not available in the United States) | None | 30 to 60 mg once daily | 60 mg (chronic pain and inflammation)<br>120 mg (acute pain for up to eight days) | ▪ May be associated with more frequent and severe dose-related cardiovascular effects (eg, hypertension) compared with nonselective and other COX-2 selective NSAIDs.<br>▪ Otherwise, risks and benefits as with celecoxib (see above). |

GI: gastrointestinal; INR: international normalized ratio; CYP450: cytochrome P450; OTC: over-the-counter, available without prescription; CrCl: creatinine clearance; COX-2: cyclooxygenase, isoform 2; CYP2C9: cytochrome 2C9; CNS: central nervous system; SSRIs: selective serotonin reuptake inhibitors.

* Available without a prescription in the United States.

¶ A list of CYP450-inducing drugs is available separately in UpToDate.

Δ NSAIDs may interact with aspirin, warfarin, methotrexate, antihypertensives, serotonin reuptake inhibitor antidepressants (eg, SSRIs, cyclic antidepressants, venlafaxine), and other drugs. For specific interactions, use the Lexi-Interact program included with UpToDate.

◇ Refer to the UpToDate topic on the cardiovascular effects of nonselective NSAIDs.

§ For additional information on gastroprotective strategies, including selective COX-2 inhibitors and other options, refer to the UpToDate topics on the overview of selective COX-2 inhibitors and on NSAIDs (including aspirin) and the primary prevention of gastroduodenal toxicity.

*Prepared with data from:*

*1. Anon. Drugs for pain. Treatment guidelines from the Medical Letter; 2013. 11:31.*

*2. Castellsague J, Riera-Guardia N, Calingaert B, et al. Individual NSAIDs and upper gastrointestinal complications: A systematic review. Drug Saf 2012; 35:1127.*



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